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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,667	04/05/2005	Vasulinga Ravikumar	ISIS-5582	4970

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EXAMINER

WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
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1635

MAIL DATE	DELIVERY MODE
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01/27/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/510,667	Applicant(s) RAVIKUMAR ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4 and 11-23 is/are pending in the application.
- 4a) Of the above claim(s) 19 and 21-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,11-18,20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 12/3/09 has been entered.

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Brian Whiteman, Art Unit 1635.

Election/Restrictions

Claims 19 and 21-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 18, 2006.

Claim Objections

Claims 17 and 18 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The range for n in claims 17 and 18 do not further limit the range for n in claim 1.

Claim 20 is objected to because of the following informalities: the phrase “an oligomeric compound of claim 1” is an improper phrase for a phrase in a dependent claim. The phrase should recite “the oligomeric compound of claim 1.” Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 11-18, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter Rejection:

The limitation 'n if from about 13 to about 23' in amended claim 1 and claims dependent therefrom is not supported by the as-filed specification. Applicant cites page 2, paragraphs 4 and 5; page 3, paragraph 9; page 4, paragraph 13; page 23, paragraph 59 and page 30, paragraph 78 for support, however, there does not appear to be a written description of the claim limitation in the application as filed. See MPEP § 2163.06. The only limitation supported in the specification are for 5 to about 50, 8 to about 30 or 15 to about 25 bases in length on page 23, paragraph 0059 and n is 3 to 48 on page 8. There does not appear to be any disclosure that would lead a skilled artisan to the limitation cited in amended claim 1.

"It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997).

Claim Rejections - 35 USC § 103

Claims 1, 4, 11-18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uhlmann (US 6,033,909, of record) in view of Kostenko et al. (Nucleic Acids Research 2001, of record), Hamma et al. (Biochemistry 1999, of record) and Sproat et al. (Nucleic Acids Research 1987, of record).

Uhlmann et al. teach oligonucleotides having formula 1 (see column 3). In this formula, the internucleotide linkages can be mono- or diphosphorothioate. The V at the 5' position of the ribose can be S and the terminal R¹ can be a phosphate group, which is the equivalent of the phosphorothioate monoester at the 5' terminus wherein the

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phosphate is attached to a 5'-thionucleotide of claim 1. The Z position of the terminal phosphate groups can be C₁-C₁₈ alkyl, meeting the limitation of claim 4. In the oligonucleotides disclosed by Uhlmann et al., R² can be hydrogen, hydroxyl or other substituents, meeting the limitations of claims 11-14. Position B is disclosed as being a conventional nucleotide base, meeting the limitations of claim 16. The oligonucleotides of Uhlmann et al. are 2-101 nucleotides in length, meeting the limitations of claims 1, 17, and 18 and are disclosed in claim 9 as compositions with pharmaceutically acceptable carrier or diluent, meeting the limitations of claim 20. Uhlmann et al. do not teach oligonucleotides having a hydroxyl or protected hydroxyl at the 3' terminus.

Kostenko et al. teach 5'-bis-pyrenylated oligonucleotides produced by conjugating pyrene to a 5' phosphorylated oligonucleotide for the purpose of producing a fluorescent probe that can quantitatively detect hybridization.

Hamma et al. teach that producing an oligonucleotide having a 5' phosphate allows a convenient "affinity handle" for purification by strong anion exchange HPLC. In view of these teachings, one of ordinary skill in the art would recognize that predictable synthesis of oligonucleotides having a 5' phosphate is routine and this technique is used for a variety of different reasons.

Sproat et al. teach the synthesis of 5'-mercapto-2', 5'-dideoxyribonucleoside phosphoramidites that can be used to produce oligonucleotides wherein the 5' oxygen is replaced with sulfur. Because these modified nucleotides are in a form suitable for automated nucleic acid synthesis, these monomers can be substituted at any position

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within an oligonucleotide, including the 5' terminus. Use of these monomers in a standard synthesis protocol produces oligonucleotides having 3' hydroxyls.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce oligonucleotides comprising 5' mercapto nucleotides and a 5' phosphate as taught by Uhlmann et al. and to make such an oligonucleotide comprising a 3' hydroxyl. Based on the teaching of Sproat et al. of 5' mercapto nucleoside phosphoramidites suitable for incorporation at any point in a synthetic oligonucleotide, one of ordinary skill in the art would recognize the use of this particular monomer to be a matter of simple substitution of known equivalents that would predictably provide 5' mercapto oligonucleotides. Based on the teachings of Kostenko et al. and Hamma et al. one of ordinary skill in the art recognizes that synthesis of 5' phosphate oligonucleotides is routine in the art, therefore the synthesis of oligonucleotides comprising both a 5' mercapto nucleotide and a 5' phosphate is a matter of design choice made in the course of routine optimization using equivalent elements known to those of ordinary skill in the art. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See **KSR v. Teleflex**, 550 U.S. ___, 127 S. Ct. 1727 (2007).

Thus, the invention of claims 1, 4, 11-18 and 20 would have been obvious, as a whole, at the time the invention was made.

Applicant's arguments filed 6/24/09 and 8/14/08 have been fully considered but they are not persuasive for the reasons set forth in the examiner's answer to appeal brief and in the final rejection mailed on 11/25/08.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number 571-272-0764. The examiner can normally be reached on from 6:30 to 4:00 (Eastern Standard Time). The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor Tracy Vivlemore can be reached on 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Brian Whiteman/
Primary Examiner, Art Unit 1635

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